E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.838

Research Article

When a Calcium Score of Zero Is Not Zero Risk: Non-Calcified Coronary Plaque and Adverse Plaque Features on Coronary Computed Tomography Angiography

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Received: 17.07.2026, Revised: 20.08.2026, Accepted: 23.08.2026

ABSTRACT
Introduction: Coronary artery calcium (CAC) scoring estimates calcified atherosclerotic burden, but a CAC score of zero does not exclude non-calcified coronary plaque or adverse plaque characteristics.
Objective: To determine the prevalence of non-calcified coronary plaque and describe reported adverse plaque features among patients with CAC=0 undergoing coronary computed tomography angiography (CCTA).
Methods: This retrospective, single-centre descriptive observational study was conducted at the Peshawar Institute of Cardiology and included CCTA examinations performed from July 2023 to June 2026. Reports were screened to identify patients with a documented CAC score of zero. Imaging findings were extracted from existing CCTA reports, and clinical risk-factor summaries were manually calculated from hospital records. Results were summarised using descriptive statistics.
Results: Among 532 patients with CAC=0 (mean age 43.7 ± 11.1 years; 296 men, 55.6%), 510 (95.9%) had no reported coronary plaque and 22 (4.1%) had non-calcified plaque. Four plaque-positive patients had reported adverse plaque features, representing 18.2% of those with non-calcified plaque and 0.8% of the entire cohort. Qualitatively described low-attenuation / hypodense morphology and positive remodelling were each reported in two patients. Spotty calcification and the napkin-ring sign were not documented.
Conclusions: Non-calcified coronary plaque was reported in 4.1% of patients with CAC=0, and a small subset had reported adverse plaque features. CCTA can identify non-calcified atherosclerosis that is not captured by calcium scoring alone. These anatomical findings do not establish independent clinical predictors or subsequent cardiovascular event risk.

Keywords: Coronary Artery Calcium, Non-Calcified Plaque, Adverse Plaque Features, Coronary Ct Angiography, Coronary Artery Disease.

INTRODUCTION

Coronary artery disease (CAD) continues to be a significant cause of morbidity and mortality in the world today, and early detection is crucial to ensure that patients who might be helped by preventive measures are identified. Coronary artery calcium (CAC) scoring is a widely adopted technique for the estimation of atherosclerotic burden and the improvement of cardiovascular risk stratification. A CAC of zero will typically have a good cardiovascular prognosis, as it means there is no detectable calcified coronary plaque. This discovery, however, does not rule out coronary atherosclerosis, especially in those with early disease who have not yet developed plaques that have calcified. An important limitation of the use of CAC scores alone for cardiovascular assessment is that recent research has shown that non-calcified coronary plaques can still be seen in those with zero CAC scores (1). A systematic review and meta-analysis by Sama et al. also looked at prevalence and clinical features of non-calcified plaque among those who were CAC score zero, highlighting the need to assess atherosclerosis beyond just coronary calcification (2).

The distinction between absence of coronary calcification and absence of coronary atherosclerosis is clinically meaningful. Lipid

accumulation, inflammation, and fibrous tissue may precede calcium deposition detectable by conventional scoring. Studies of lipid markers have explored whether biochemical characteristics help identify plaque in patients with CAC=0 (3). Reviews of the clinical implications of a zero score also emphasise interpreting CAC alongside clinical presentation and cardiovascular risk factors (4).

CCTA depicts the coronary lumen and plaque morphology beyond the calcium measurement. Research on detailed plaque analysis in patients with chest pain and CAC=0 illustrates the distinction between calcium scoring and assessment of the coronary artery wall (5). Evidence concerning CAC detected on non-gated thoracic CT addresses the value of coronary calcium in another imaging setting (6). Calcium assessment alone, however, does not characterise non-calcified coronary plaque.

Of particular importance is the non-calcified coronary plaque because its clinical relevance is determined by the extent, composition and morphology of the plaque. Depending on the biological behavior and the patient risk factors of such plaques, they may lead to narrowing of the lumen and progressive atherosclerosis and acute coronary syndromes. The literature available has focused on the prevalence, diagnostic evaluation and prognostic value of non-calcified plaque in patients with symptoms and those without symptoms, making CCTA an important modality to use in the study of coronary disease not captured by calcium scoring (7). Incorporating CAC scoring with CCTA may be able to give complementary information that can help the clinician distinguish those with no visible coronary plaque from those with non-calcified atherosclerosis who have an apparently reassuring calcium result. This integrated approach could also facilitate more personalized cardiovascular preventive and therapeutic decisions in patients where traditional risk factors and clinical presentation indicate residual risk (8).

It is also important to consider the clinical population under study when interpreting a zero calcium score. Studies on the value of screening for coronary artery disease in asymptomatic persons indicate that the benefit of computed tomography is dependent on the risk level of the patient's baseline condition, the diagnostic utility of the scan, and the likelihood of the results affecting preventive treatment (9). In addition, the diagnostic performance of CAC=0 can differ in populations, clinical settings, and demographic groups. The diagnostic value of zero calcium score in a Malaysian cohort of patients referred for evaluation of coronary artery disease was reviewed in a retrospective analysis, which stressed the need to interpret the results in the context of the population being evaluated and not in isolation (10). Interest in the wider predictive use of the CAC has also grown, with studies focusing on its association with systemic disease and risk assessment, although coronary plaque assessment is clearly a separate need when there is a primary interest in the absence of known coronary atherosclerosis (11).

Demographic and cardiovascular risk factors provide relevant context when interpreting coronary imaging. Studies of low-attenuation plaque burden have examined clinical determinants of plaque composition (12), while research on non-gated chest CT has considered the value of coronary calcification for risk stratification (13). Describing the clinical characteristics of patients with CAC=0 and their CCTA findings can help characterise the population in which non-calcified disease is identified.

Adverse plaque features described on CCTA include low attenuation, positive remodelling, spotty calcification and the napkin-ring sign. Studies such as ICONIC have examined plaque characteristics in relation to acute coronary syndrome among patients with CAC=0 (14). Research on non-obstructive coronary disease and the SCOT-HEART cohort provides further context for interpreting plaque findings alongside clinical risk factors and CAC burden (15,16). These outcome-based studies differ from a descriptive analysis of existing reports without clinical follow-up.

Pakistani data on discordance between calcium burden and coronary disease severity provide a regional context for this question (17). Reviews of emerging CAC applications also highlight the distinction between calcium assessment and more detailed coronary imaging (18). A single-centre study at the Peshawar Institute of Cardiology can contribute local information on non-calcified plaque and reported adverse plaque features among patients with CAC=0.

Objective: To determine the prevalence of non-calcified coronary plaque and describe reported adverse plaque features among patients with CAC=0 undergoing CCTA at the Peshawar Institute of Cardiology, Peshawar, Pakistan.

MATERIALS AND METHODS

Study Design: This was a retrospective, single-centre descriptive observational study of CCTA examinations.

Study Setting and Ethics: The study was conducted at the Peshawar Institute of Cardiology, Peshawar, Pakistan. Ethical approval was obtained for this retrospective study.

Study Period: CCTA examinations performed from July 2023 to June 2026 were included.

Inclusion Criteria: All available CCTA reports during the study period were screened. Patients with an explicitly documented total Agatston CAC score of zero were included in the analytic cohort.

Exclusion Criteria: Reports of patients with previous coronary artery bypass grafting (CABG) and exact duplicate reports were excluded. Reports without an explicitly documented CAC score were not assumed to represent CAC=0. Patients with CAC>0 were excluded from the CAC-zero analysis.

Data Collection: Demographic, clinical and imaging information was collected using a standardised data collection framework. Demographic variables included age and sex. Clinical risk-factor summaries for hypertension, diabetes mellitus, dyslipidaemia, current smoking and family history of premature coronary artery disease were manually calculated from hospital records. Imaging findings were obtained from existing CCTA reports, and the original CT images were not re-reviewed for this study. Patient and plaque-feature counts were manually checked by the investigator. Undocumented clinical information was not automatically classified as negative.

Imaging Definitions: The total Agatston CAC score was extracted as reported. Non-calcified plaque was recorded when the CCTA report explicitly described non-calcified, soft-tissue or equivalent coronary atherosclerotic plaque. Anomalous coronary anatomy, myocardial bridging, vessel hypoplasia, and extrinsic compression were not classified as non-calcified plaque. Low-attenuation/hypodense morphology, positive remodelling, spotty calcification and the napkin-ring sign were recorded when described in the report. Qualitative hypodense descriptions were retained as reported and were not assumed to satisfy a quantitative attenuation threshold. Individual adverse plaque features were distinguished from an independently verified high-risk plaque classification. An unmentioned feature was considered not documented rather than confirmed absent.

Statistical Analysis: Analyses were descriptive. Age was summarised as mean ± standard deviation. Categorical findings were presented as counts and percentages where exact counts were available; clinical risk factors were presented as the rounded percentages manually calculated from hospital records. Non-calcified plaque prevalence used all 532 patients with CAC=0 as the denominator. Adverse plaque findings were expressed relative to the 22 plaque-positive patients and, where indicated, the entire cohort. No inferential comparison between plaque groups or multivariable predictor analysis was performed.

RESULTS

The cohort selection is shown in Figure 1. Among 532 patients with CAC=0, 510 (95.9%) had no reported coronary plaque and 22 (4.1%) had non-calcified plaque. Four plaque-positive patients had reported adverse plaque features, representing 18.2% of the plaque-positive subgroup and 0.8% of the entire cohort. Baseline characteristics are summarised in Table 1 and individual plaque-feature frequencies in Table 2.

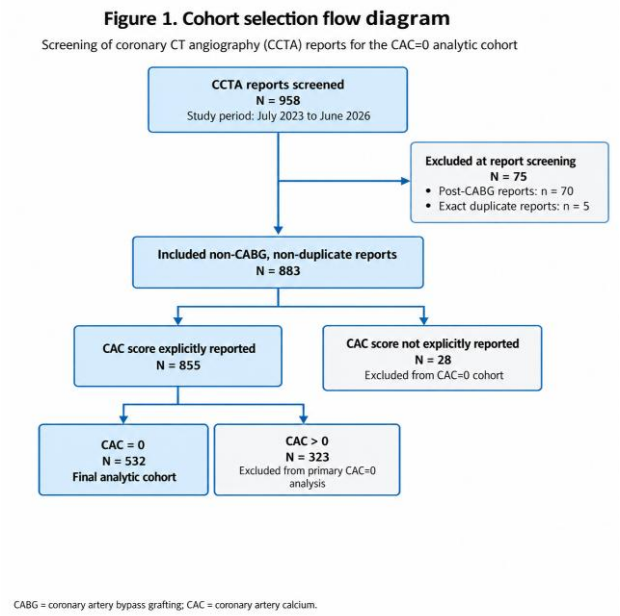


Figure 1. Cohort selection flow diagram: screening of CCTA reports for the CAC=0 analytic cohort.

During the study period, 958 CCTA reports were screened. Seventy-five reports were excluded: 70 post-CABG reports and five exact duplicate reports, leaving 883 eligible reports. Of these, 28 lacked an explicitly documented CAC score and were excluded from the CAC-zero analysis. Among the remaining 855 reports, 532 (62.2%) had CAC=0 and 323 (37.8%) had CAC>0. The final CAC-zero cohort comprised 532 patients. The CAC>0 group was not analysed for plaque prevalence or compared with the CAC-zero cohort.

Table 1. Demographic and clinical characteristics and plaque findings in patients with CAC=0 (n=532)

Characteristic	Overall, n (%) / Mean ± SD
Age, years	43.7 ± 11.1
Male sex	296 (55.6%)
Female sex	236 (44.4%)
Hypertension	37%
Diabetes mellitus	29%
Dyslipidaemia	28%
Current smoking	18%
Family history of premature CAD	14%
Non-calcified/soft-tissue plaque on CCTA	22 (4.1%)
Reported adverse plaque features among plaque-positive patients	4/22 (18.2%)

The mean age was 43.7 ± 11.1 years. There were 296 men (55.6%) and 236 women (44.4%). Hypertension was present in 37%, diabetes mellitus in 29%, dyslipidaemia in 28%, current smoking in 18%, and family history of premature CAD in 14%. Non-calcified plaque was reported in 22 patients (4.1%); four of these patients (18.2%) had reported adverse plaque features.

Table 2. Reported adverse plaque features among patients with non-calcified plaque (n=22)

Adverse plaque feature	Reported, n (%)
Qualitatively described low-attenuation/hypodense morphology	2 (9.1%)
Positive remodelling	2 (9.1%)
Spotty calcification	0 documented
Napkin-ring sign	0 documented

Qualitatively described low-attenuation/hypodense morphology was reported in two patients and positive remodelling in two patients (9.1% of plaque-positive patients for each feature). The manually verified patient-level count was four patients with reported adverse features. Spotty calcification and the napkin-ring sign were not documented. These findings describe report-documented morphology and do not establish that unmentioned features were systematically assessed and absent on the original images.

DISCUSSION

This single-centre study found non-calcified coronary plaque in 22 of 532 patients with CAC=0 (4.1%). Most patients had no reported coronary plaque, while four plaque-positive patients had reported adverse morphological features. The principal finding is that a zero calcium score can coexist with non-calcified coronary atherosclerosis; it does not establish a high prevalence of plaque or an increase in subsequent clinical events.

The coexistence of CAC=0 and non-calcified plaque is consistent with previous work distinguishing absence of detectable calcium from absence of atherosclerosis (1,2,4,7). Published prevalence estimates depend on population characteristics, referral indications and imaging assessment methods. The meta-analysis by Sama et al. concerns asymptomatic individuals (2), whereas the present study describes patients referred to a tertiary cardiac centre. Direct numerical comparisons should therefore be made cautiously. Extraction from existing reports may also yield different estimates from systematic review of the original images.

Lipid-marker research provides a biological context for plaque formation before calcium becomes detectable (3). The present study describes the frequencies of hypertension, diabetes, dyslipidaemia, smoking and family history in the CAC-zero cohort. These overall frequencies do not establish associations with plaque presence. Because no inferential comparison between plaque-positive and plaque-negative patients or adjusted analysis was performed, no clinical characteristic can be identified as an independent predictor from these results.

The adverse-feature findings require careful interpretation. Low-attenuation/hypodense morphology and positive remodelling were each reported in two patients, and four patients had reported adverse features overall. These patients represented 18.2% of the plaque-positive subgroup and 0.8% of the entire cohort. The presence of an individual adverse description is not equivalent to independently demonstrating a formally defined high-risk plaque phenotype. No report documented spotty calcification or the napkin-ring sign, but non-documentation does not establish that these features were assessed and absent. Studies relating plaque composition to outcomes provide context (12,14,16), although their measurements and endpoints differ from this descriptive report-based analysis.

CCTA and calcium scoring describe related but different aspects of coronary atherosclerosis. Studies of detailed plaque analysis and reviews of imaging in prevention illustrate the additional anatomical information available from CCTA (5,8). This study did not assess treatment changes, diagnostic accuracy against an independent reference standard, or clinical outcomes. Its findings therefore do not establish a benefit from routine CCTA in every patient with CAC=0. The use of further imaging should be considered in the context of clinical presentation and established indications.

Evidence concerning asymptomatic screening, population-specific diagnostic assessment and non-obstructive coronary disease illustrates the importance of clinical context (9,10,15). The present cohort was drawn from one tertiary cardiac centre and should not be regarded as representative of Khyber Pakhtunkhwa or Pakistan. Regional work on discordance between CAC burden and coronary disease severity supports the relevance of this question (17), but does not substitute for a directly comparable analysis. The present study did not compare plaque prevalence between CAC=0 and CAC>0 patients.

Research on opportunistic calcium assessment on non-gated thoracic CT highlights the increasing availability of coronary calcium information (6,13,18). Broader applications of CAC scoring have also been investigated beyond coronary outcomes (11). The present findings address a narrower anatomical question: whether non-calcified plaque is reported on CCTA despite a total Agatston score of zero. Differences in scan protocols, populations and endpoints limit direct comparison with opportunistic screening studies.

This study has several limitations. Its retrospective, single-centre design and clinically referred population limit generalisability. Imaging findings were extracted from existing

reports without independent re-review of the CT images; differences in reporting detail may therefore affect ascertainment of plaque and adverse features. Absence of a documented feature does not establish its absence on the images. Quantitative attenuation and remodelling measurements were not available in the presented analysis, and the number of plaque-positive patients was small. Clinical risk-factor frequencies were descriptive and were not analysed in relation to plaque status. Clinical follow-up was unavailable, so the prognostic significance of the observed findings could not be determined.

Future studies using standardised clinical data, systematic image assessment and longitudinal follow-up could clarify the determinants and prognostic significance of non-calcified plaque in patients with CAC=0. Within the present descriptive scope, the findings demonstrate that a zero calcium score does not exclude non-calcified atherosclerosis reported on CCTA.

CONCLUSION

Among 532 patients with CAC=0, non-calcified coronary plaque was reported in 22 (4.1%). Four patients had reported adverse plaque features, representing 18.2% of plaque-positive patients and 0.8% of the entire cohort. These findings demonstrate that a zero CAC score does not exclude non-calcified coronary atherosclerosis. CCTA provides anatomical information beyond calcium scoring, but independent clinical predictors and the prognostic significance of the observed plaque features were not established in this descriptive study.

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